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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/530,234	07/06/2000	JOHN D. STEEVES	MBM1200	3942

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EXAMINER	
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ART UNIT	PAPER NUMBER
1646	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/530,234	STEEVES ET AL.
	Examiner	Art Unit
	Olga N. Chernyshev	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 2,4,6,16-18,29,30,32 and 35-54 is/are pending in the application.

4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 36,38,40,43,44,46,48 and 49 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6, 7, 9 OC
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continuation of Disposition of Claims: Claims withdrawn from consideration are 2,4,6,16-18,29,30,32,35,37,39,41-43,47,50 and 52-54.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in Paper No.11 is acknowledged.

Claims 2, 4, 6, 16-18, 29-30, 32 and 35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No.11.

2. Claims 1, 3, 5, 7-15, 19-28, 31, 33 and 34 have been cancelled and claims 36-54 have been added as requested in the amendment of paper No.11.

Newly submitted claims 37, 39, 41-42, 45, 47, 50 and 52-54 are directed to inventions that are independent or distinct from the invention originally claimed for the following reasons: claims 37, 39, 41, 43, 47 and 50 are drawn to the inventions of original Groups II or III and claims 42 and 52-54 are drawn to invention of original Group III (see the office action of Paper No.8).

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 37, 39, 41-42, 45, 47, 50 and 52-54 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 36, 38, 40, 43, 44, 46, 48, 49 and 51 are under examination in the instant office action.

Priority

3. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(a)-(d) based upon an applications filed in Canada on 10/28/1997 and 10/16/1998. A claim for priority under 35 U.S.C. 119(a)-(d) cannot be based on said application, since the United States application was filed more than twelve months thereafter.

If applicant desires priority under 35 U.S.C. 365 (c) based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed on or after November 29, 2000, any claim for priority must be made during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2) and (a)(5). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c).A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by

(1) a surcharge under 37 CFR 1.17(t), and (2) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Commissioner may require additional information where there is a question whether the delay was unintentional. The petition should be directed to the Office of Petitions, Box DAC, Assistant Commissioner for Patents, Washington, DC 20231.

Drawings

4. The drawings filed on July 06, 2000 are acceptable subject to correction of the informalities indicated on the attached "Notice of Draftperson's Patent Drawing Review," PTO-948. In order to avoid abandonment of this application, correction is required in reply to the Office action. The correction will not be held in abeyance.

Specification

5. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

6. Claim 43 is objected to because of the following informalities: claim does not end with a period.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claim 36 rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

Claim 36 is directed to a method for inducing transient disruption of myelin and/or demyelination in mammalian neurological tissue in the CNS of a subject. As it is well known in the art, multiple sclerosis (MS) is a neurodegenerative debilitating disease characterized by widespread demyelinated lesions in central nervous system accompanied by inflammatory cell infiltrates. According to the claim 36, the claimed invention is directed to a method for inducing demyelination which can lead to a serious neurological condition and potentially incapacitating disease, MS, in a subject. Therefore, the invention as claimed in claim 36 does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 36, 38, 43, 44, 46 and 48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inducing transient disruption of myelin in rodent neurological tissue, does not reasonably provide enablement for the same method practiced in any mammalian subject. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 36, 38 and 43-44 are directed to a method for inducing transient disruption of myelin in mammalian neurological tissue of a subject. Claims 46 and 48 are directed to a method for promoting neuron repair by transient demyelination. The instant specification describes the principle of the invention, which relays on discovery that transient disruption of myelin by administration of a complement-fixing myelin-specific antibody in combination with compliment proteins can be beneficial during neuronal regeneration because this process is usually greatly inhibited by the presence of certain components located or embedded in myelin (see page 5, third paragraph and page 17, seventh paragraph of the instant specification, for example). However, the instant specification fails to provide enough guidance how to practice the claimed methods in mammals other than rodents, thereby requiring undue experimentation to discover how to make and use the full scope of Applicant's invention, as currently claimed.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. In re Wands, 8 USPQ2d, 1400 (CAFC 1988).

Claims 36, 38, 43, 44, 46, 48 are drawn to a method of treatment by administration of composition of antibodies and complement proteins. The art of treating diseases, disorders or conditions by administration of immunologically active proteins and antibodies is generally

considered to be unpredictable. Numerous publications exist on a topic of unsuccessful human trials of treating conditions with such proteins like, for example, growth factors (see, for example, "Neurotrophic factors enter the clinic", Science, 1994, 264, pp.772-774, whole paper). The instant specification clearly fails to supply the guidance that would be needed by a routine practitioner on how to extrapolate data obtained from experiments on rodent model and exercise the same method in any mammal, including a human. One skilled in the art would not expect findings obtained from a rodent model be predictive of successful treatment of a human.

To practice such a method would require knowledge of the route, duration and quantity of administration of combination of antibodies and compliment proteins to a subject and this information is not provided by the instant specification. The instant specification has also failed to disclose how these parameters are to be determined, how a similar method was practiced in the art with a different agent or to provide even a single working example, prophetic or actual, of the claimed method practiced in a mammal other than a rat. In the absence of this guidance a practitioner would have to resort to a substantial amount of undue experimentation involving the variation in the amount and duration of administration of combination of antibodies and compliment proteins of the instant invention and in determining a suitable route of administration. The instant situation is directly analogous to that which was addressed in *In re Colianni*, 195 U.S.P.Q. 150,(CCPA 1977), which held that a "[d]isclosure that calls for application of "sufficient" ultrasonic energy to practice claimed method of fusing bones but does not disclose what "sufficient" dosage of ultrasonic energy might be or how those skilled in the art might select appropriate intensity, frequency, and duration, and contains no specific examples or

embodiment by way of illustration of how claimed method is to be practiced does not meet requirements of 35 U.S.C. 112 first paragraph".

Thus, in view of the lack of teachings and unpredictability of the art set forth earlier, and also the lack of the working examples, the instant specification is not found to be enabling for a method for inducing transient disruption of myelin in mammalian neurological tissue. It would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to practice the full scope of Applicant's invention as currently claimed.

9. Claims 40, 49 and 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 40, 49 and 51 are directed to a method for treating a nervous system dysfunction in a mammalian subject by administration of complement-fixing antibodies in combination with complements proteins. Note that although the "nervous system dysfunction" is not limited to a neuronal regeneration, with regard to claims breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the enablement scope of the claims, the teachings of the specification are to be taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification. As such, the broadest reasonable interpretation of the claimed invention is a method for treating a nervous system dysfunction, including trauma and degeneration, for example. The instant specification fails to present enough guidance for the claimed method for the reasons explained earlier. Further, one

skilled in the art would not expect that treatment by administration of complement-fixing antibodies in combination with complements proteins would benefit all or any dysfunctions of nervous system. Taking into consideration that administration of anti-myelin antibodies in combination with complement proteins causes demyelination of nervous tissue, a potentially serious pathological condition, a skilled practitioner needs to know precise protocol in order to practice the claimed invention, and such protocol is not supplied by the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 36, 38, 40, 43, 44, 46, 48, 49 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claims 36, 43, 46, 48, 49 and 51 are indefinite for being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the step that indicates the induction of myelin disruption (claims 36 and 43), or neuron regeneration (claim 46), or treatment of nervous system dysfunction (claims 49 and 51).

12. Claim 36 is further indefinite and ambiguous for recitation of "an immunological activating agent". The metes and bounds of this recitation cannot be determined from the claim.

13. Claims 36 and 46 are indefinite for the "and/or" statements. For example, claim 36 may encompass a) a method for inducing transient disruption of myelin and inducing demyelination; b) a method for inducing transient disruption of myelin and inducing transient disruption of

demyelination; c) a method for inducing transient disruption of myelin or inducing demyelination; or d) a method for inducing transient disruption of myelin or inducing transient disruption of demyelination. Clarification id required.

14. Claims 43 and 46 are vague and indefinite for reciting "therapeutically effective amounts". It is not clear and cannot be determined from the claims or the instant specification what amounts of complement-fixing antibodies and complement proteins are considered to be "therapeutically effective" and in what proportion within the composition. Is it combination of "therapeutically effective amounts" of antibodies and "therapeutically effective amounts" of complement proteins or is it "therapeutically effective amounts" of combination of both (or more?).

15. Claims 46 and 49 are vague and ambiguous for recitation of "demyelination of myelin". Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 36, 38, 40, 43, 46 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Dyer et al. (1995, Society for Neuroscience Abstracts, IDS of Paper No.6).

Dyer et al. teach administration of complement proteins and myelin-specific antibodies (immunological activating agents), which induced transient disruption of myelin in mice (a

mammal), thus meeting the limitations of claims 36 and 38. Dyer et al. also describe the invention of claim 40, wherein neuronal disruption is interpreted as "nervous system dysfunction", and claims 43, 46 and 49 because the steps recited in therein are the same as disclosed in teachings of Dyer et al. (see the whole document).

17. Claim 46 is also rejected under 35 U.S.C. 102(b) as being anticipated by Keirstead et al. (1992, reference AI of the IDS of Paper No.6).

Keirstead et al. teach neuroanatomical repair and functional recovery of thoracic cord of an embryonic chicken after demyelination caused by injection of an IgG3 mouse GalC antibody plus 20% homologous serum as a source of complement (see abstract and p.11664, second column, paragraph "Dysmyelination").

Conclusion

18. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D. oc
April 30, 2002

CHRISTINE J. SAOUD
PRIMARY EXAMINER
Christine J. Saoud

Attachment for PTO-948 (Rev. 03/01, or earlier)
6/18/01

The below text replaces the pre-printed text under the heading, "Information on How to Effect Drawing Changes," on the back of the PTO-948 (Rev. 03/01, or earlier) form.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the Notice of Allowability. Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136(a) or (b) for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a).

Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.